INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/15621

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 70.1, 320.1, 325, 455; 514/2; 530/350; 536/23.1, 23.5, 24.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	IWANE. M. et al. Production, Purification And Characterization of Biologically Active Recombinant Human Nerve Growth Factor. Biochem. Biophys. Res. Comm. 31 August 1990. Vol. 171. No. 1. pages 116-122, see entire document.	1-3, 8-11, 13, 14, 16-21, 23, 24, 29, 30, 49 --- 4, 22, 25, 31
X --- Y	KHURSIGARA. G. et al. Association of the p75 Neurotrophin Receptor with TRAF6. J. Biol. Chem. 29 January 1999. Vol. 274. No. 5. pages 2597-2600, see entire document.	1-3, 8-11, 13, 14, 16-21, 23, 24, 29, 30, 49 --- 4, 22, 25, 31

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

06 NOVEMBER 2000

Date of mailing of the international search report

07 DEC 2000

Name and mailing address of the ISA/US
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Form PCT/ISA/210 (second sheet) (July 1998) ★

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	FAINZILBER. M. et al. CRNF, a Molluscan Neurotrophic Factor That Interacts with the p75 Neurotrophin Receptor. Science. 29 November 1996. Vol. 274. pages 1540-1543, see entire document.	29, 30 --- 1-4, 8-11, 13, 14, 16-25, 31, 49
X,E	MUKAI. J. et al. NADE, a p75NTR-Associated Cell Death Executor, is Involved in Signal Transduction Mediated by the Common Neurotrophin Receptor p75NTR. J. Biol. Chem. 09 June 2000. Vol. 275. No. 23. pages 17566-17570, see entire document.	1-5, 8-11, 13, 14, 16-25, 29-31, 35, 49

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please see extra sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-25, 29-38, 49, 53 and 54

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

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1. This International Search Authority has found 22 inventions claimed in the International Application covered by the claims indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-25, 29-38, 49, 53, and 54 drawn to isolated nucleic acid molecules encoding a polypeptide capable of binding a p75ntr receptor, vectors, host cells, methods of using the isolated nucleic acid molecules to produce polypeptides, and polypeptides.
Group II, claim(s) 26-28, drawn to antisense oligonucleotides.
Group III, claim(s)39-42, drawn to antibodies.
Group IV, claim(s) 43-45, drawn to a method of inducing apoptosis in cells comprising expressing a polypeptide capable of binding p75ntr receptor in cells.
Group V, claim(s) 46-48, drawn to a transgenic nonhuman mammal comprising a nucleic acid molecule encoding a polypeptide capable of binding a p75ntr receptor and a method of using the transgenic animal.
Group VI, claim(s)50-52, drawn to a method of inducing apoptosis of cells in a subject comprising administering a purified polypeptide capable of binding p75ntr receptor.
Group VII, claim(s) 55-68, drawn to a method of identifying a compound capable of inhibiting binding between p75ntr receptor and a polypeptide capable of binding the receptor.
Group VIII, claim(s) 69-72, drawn to a method for identifying an apoptosis-inducing compound.
Group IX, claim(s)73-77, drawn to a method for screening cDNA libraries of a polypeptide capable of binding p75ntr receptor.
Group X, claim(s) 78, drawn to a method to induce caspase-2 and caspase-3 activity requiring co-expression of the p75ntr receptor and a receptor-binding ligand.
Group XI, claim(s) 79, drawn to a method to inhibit NF-kB activation in a cell with a polypeptide capable of binding p75ntr receptor and p75ntr.
Group XII, claim(s)80-82, drawn to a method for detecting neurodegenerative disease by detecting expression levels of p75ntr and a polypeptide capable of binding p75ntr receptor.
Group XIII, claim(s) 83-85, drawn to a transgenic nonhuman mammal comprising a polynucleotide encoding a human HGR74 protein, and a method of using the transgenic mammal.
Group XIV, claim(s)86, and 90, drawn to a method of producing human HGR74 protein.
Group XV, claim(s) 87-89, drawn to a method of inducing apoptosis in a subject comprising administering purified human HGR74 protein.
Group XVI, claim(s) 91-94, drawn to a method for identifying an apoptosis inducing compound comprising measuring the expression levels of human HGR74 and p75ntr.
Group XVII, claim(s)95-99, drawn to a method for screening cDNA libraries for human HGR74 protein.
Group XVIII, claim(s) 100, drawn to a method to induce caspase-2 and caspase-3 activity by co-expression of human HGR74 protein and p75ntr.
Group XIX, claim(s) 101, drawn to a method to inhibit NF-kB activation in a cell with human HGR74 protein and p75ntr.
Group XX, claim(s)102-104, drawn to a method for detecting neurodegenerative disease by detecting expression levels of human HGR74 protein and p75ntr.
Group XXI, claim(s) 105-130, drawn to a method of identifying an apoptosis inhibitor.
Group XXII, claim(s) 131-137, drawn to isolated nucleic acid molecules encoding deletion mutants of neurotrophin associated cell death executor protein.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:
This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

a polypeptide capable of binding p75ntr receptor is
a. a neurotrophin associated cell death executor
b. a human HGR74 protein
c. a musnade3a sequence
d. a hunade3a1 sequence
e. a hunade3a2 sequence
f. a ratnad3a sequence

g. a ratnad3b sequence
h. a musnade3a sequence
i. a musnade3b sequence
j. a humnade1 sequence
k. a ratnade1 sequence
l. a musnade1 sequence
m. a humnade2 sequence

The claims are deemed to correspond to the species listed above in the following manner:

a. a neurotrophin associated cell death executor- claims 57 and 117
b. a human HGR74 protein- claims 58 and 118
c. a musnade3a sequence- claims 59 and 119
d. a hunade3a1 sequence- claims 60 and 120
e. a hunade3a2 sequence- claims 61 and 121
f. a ratnad3a sequence- claims 62 and 122
g. a ratnad3b sequence- claims 63 and 123
h. a musnade3a sequence- claim 124
i. a musnade3b sequence- claims 64 and 125
j. a humnade1 sequence- claims 65 and 126
k. a ratnade1 sequence- claims 66 and 127
l. a musnade1 sequence- claims 67 and 128
m. a humnade2 sequence- claims 68 and 129

The following claims are generic: 55, 56 and 105

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

an apoptosis inhibitor which can be
a. an antibody
b. an inorganic compound
c. an organic compound
d. a peptide, peptidomimetic, polypeptide or protein

The claims are deemed to correspond to the species listed above in the following manner:

a. an antibody - claim 110
b. an inorganic compound - claim 110
c. an organic compound - claim 110
d. a peptide, peptidomimetic, polypeptide or protein - claim 110

The following claim is generic: 105

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (7):

A61K 38/00; C07H 21/02, 21/04; C07K 14/00; C12N 5/00, 5/06, 5/10, 15/00, 15/09, 15/11, 15/12, 15/63

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

435/69.1, 70.1, 320.1, 325, 455; 514/2; 530/350; 536/23.1, 23.5, 24.1

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

INTERNATIONAL SEARCH REPORT

International application No.
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WEST, MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS
search terms: low affinity neurotrophin receptor, neurotrophin associated cell death executer protein, nade, hgr74, neurotrophin growth factor, ngf, ngf and cDNA